AMENDMENT TO THE CLAIMS

A listing of the claims presented in this patent application appears below. This listing replaces all prior versions and listing of claims in this patent application.

Claim 1 (original): A method of identifying a secondary target site comprising:

(a) providing a plurality of cells having a genome, which includes at least one primary gene encoding telomerase activity and a promoter that can direct the over expression of said primary gene;

(b) effecting one or more mutations in the genome of said cells, at one or more secondary sites;

(c) selecting those cells having at least one mutation that proves lethal to said cells when said primary gene is over expressed;

(d) determining a site in the genome of said cells in which said at least one lethal mutation is located, to provide a secondary target site.

Claim 2 (currently amended): The method of claim 1 in which said secondary target site includes a *tol* gene, a homolog thereof, or an analog thereof[[,]] ~~including mammalian homologs or analogs thereof~~.

Claim 3 (currently amended): The method of claim 2 in which said *tol* gene is selected from the group consisting of *tol1, tol2, tol3,* a homolog thereof, or an analog thereof[[,]] ~~including mammalian homologs or analogs thereof~~.

Claim 4 (original): The method of claim 1 in which said secondary target site or any gene product thereof is involved in either the modulation of the expression of said primary gene or a process affecting the viability of the cell in which said primary gene is over expressed.

Claim 5 (currently amended): The method of claim 1 in which said at least one primary gene is selected from the group consisting of *ESTl, EST2, EST3, TLCl,* a homolog thereof, an analog thereof, ~~including mammalian homologs or analogs thereof~~ [or] and combinations thereof.

Claim 6 (original): The method of claim 2 in which a homolog or an analog of said *tol* gene is selected from the group consisting of *CHLl,* a gene encoding human helicase, *ercc2,* a gene encoding mouse DNA helicase, or a gene encoding human type II keratin subunit protein.

Claim 7 (currently amended): The method of claim 5 in which said *TLCl* gene is selected from the group consisting of *embZ35904, gbUl4595, embZ35905, dbjD28120, gbL24113, embX76992, gbACOO5476.3, gbU53340,* ~~including mammalian homologs or analogs thereof~~ [or] and combinations thereof.

Claim 8 (currently amended): The method of claim 5 in which said *ESTl, EST2,* and *EST3* genes are selected from those genes encoding human kininogen HMW heavy chain, prepro alpha-2thiol proteinaise, calmodulin-stimulated protein, kininogen, immunoglobulin kappa chain, nitric-oxide synthase, immunoglobulin heavy chain variable, T-cell receptor deltachain V, Ig gamma-chain, Ig H-chain V-D-JH4-region, perlecan, insulin-like growth factor II, interferon-alpha, rat coding sequence of p15 and p12, interferon-alpha I precursor, AAD10, [or] and combinations thereof.

Claim 9 (currently amended): The method of claim 1, which further comprises ~~using~~ screening said secondary target site, or lethal mutations thereof, ~~to screen~~ for a drug or drug candidate that interacts with, binds to, or inhibits the activity of a gene product associated with said secondary target site.

Claim 10 (original): The method of claim 9 in which said drug or drug candidate inhibits the growth or replication of a human tumor or causes the demise of said human tumor.

Claim 11 (canceled).

Claim 12 (original): The method of claim 9 in which said drug or drug candidate comprises a polypeptide, an oligonucleotide, a polysaccharide, or a small molecule.

Claim 13 (canceled).

Claim 14 (canceled).

Claim 15 (currently amended): A method of inhibiting the growth or replication of a tumor cell or causing the demise of said cell, said cell comprising a *tol* gene or an analog or homolog of a *tol* gene and exhibiting aberrant telomerase activity, comprising administering a drug or drug candidate that interacts with, binds to, or inhibits the expression or activity of ~~a gene product associated with a secondary target site in the genome of said cell, which site can accommodate at least one mutation that can prove lethal to said cell~~ the *tol* gene or homolog or analog of a *tol* gene.

Claim 16 (canceled).

Clam 17 (currently amended): The method of claim 15 in which said *tol* gene is selected from the group consisting of *tol1*, *tol2*, *tol3*, a homolog thereof, or an analog thereof[[,]] ~~including mammalian homologs or analogs thereof~~.

Claim 18 (original): The method of claim 15 in which said aberrant telomerase activity comprises overexpression of telomerase.

Claim 19 (canceled).

Claim 20 (canceled).

Claim 21 (currently amended): A recombinant eukaryotic cell comprising at least one secondary target site, ~~a homolog thereof, or an analog thereof~~ and at least one primary gene[[,]]~~a homolog thereof, or an analog thereof, wherein said at least one primary gene~~ which encodes telomerase, wherein ~~and~~ said at least one secondary target site contains a mutation such that the up regulation, down regulation, elimination, or disruption of said at least one primary gene gives rise to senescence or synthetic lethality.

Claim 22 (original): A method of screening for drugs, comprising:

(a) providing one or more eukaryotic cells capable of telomerase overexpression, which one or more cells exhibit senescence or synthetic lethality under conditions of telomerase overexpression when a wild-type *tol* gene, its homolog, or its gene product of said one or more cells is mutated;

(b) contacting said one or more cells with one or more drug candidates under conditions that provide telomerase overexpression and, optionally, inhibition or mutation of said wild-type *tol* gene, its homolog, or its gene product; and

(c) selecting those drug candidates that give rise to senescence or synthetic lethality under conditions that provide telomerase overexpression or those drug candidates that inhibit, suppress, reverse, or prevent senescence or synthetic lethality under conditions that provide telomerase overexpression and inhibition or mutation of said wild-type *tol* gene, its homolog, or its gene product.

Claim 23 (canceled).

Claim 24 (currently amended): A method of inhibiting the growth or replication of a tumor cell or causing the demise of said cell, said cell exhibiting aberrant telomerase activity and comprising a *tol* gene or an analog or homolog thereof, said method comprising the step of administering a drug or drug candidate that interacts with, binds to, or inhibits (or enhances) the expression or activity of a gene product associated with the ~~secondary target site of claim 21~~ *tol* gene or homolog or analog thereof.

Claim 25 (currently amended): A pharmaceutical composition comprising an effective amount of a drug or drug candidate and a pharmaceutically acceptable carrier or diluent, said drug or drug candidate capable of interacting with, binding to, or inhibiting (or enhancing) the expression or activity of a gene product associated with ~~the secondary target site of claim 21~~ a *tol* gene or homolog or analog thereof.

Claim 26 (currently amended): The pharmaceutical composition of claim 25 in which said ~~secondary target site~~ *tol* gene or homolog or analog thereof is found in the genome of a cell exhibiting aberrant telomerase activity.

Claim 27 (original): The pharmaceutical composition of claim 25 in which said aberrant telomerase activity comprises overexpression of telomerase.

Claim 28 (currently amended): A method of inhibiting the growth or replication of a tumor cell or causing the demise of said cell, said cell exhibiting aberrant telomerase activity, comprising administering a drug or drug candidate that interacts with, binds to, or inhibits (or enhances) the expression or activity of a gene product associated with ~~a secondary target site~~ *tol* gene or homolog or analog thereof.

Claim 29 (currently amended): A pharmaceutical composition comprising an effective amount of a drug or drug candidate and a pharmaceutically acceptable carrier or diluent, said drug or drug candidate capable of interacting with, binding to, or inhibiting the expression or activity of a gene product associated with a ~~secondary target site~~ tol gene or an analog or homolog thereof in the genome of a cell exhibiting aberrant telomerase activity.

Claim 30 (original): The pharmaceutical composition of claim 29 in which said aberrant telomerase activity comprises overexpression of telomerase.